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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/750,410	12/28/2000	Gloria C. Li	55672-A-PCT-US/ JPW/AJM/M	6916

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EXAMINER	
ZARA, JANE J	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 12/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/750,410	LI ET AL.	
	Examiner	Art Unit	
	Jane Zara	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,15,16 and 18-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,15,16 and 18-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6-4-02, 10-4-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *sequence non-compliance*.

DETAILED ACTION

This Office action is in response to the communication filed 10-4-04.

Claims 1, 2, 15, 16, 18-24 are pending in the instant application.

Specification

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. **Please provide appropriate accompanying SEQ ID Nos. for the sequences in the specification and figures (see e.g. p. 24 last paragraph, p. 25, middle paragraph, and p. 26, first paragraph of the specification; see also figure 14).** See the accompanying Notice to Comply.

Maintained Rejections

Double Patenting

Claims 1-16, 18-24 provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-24 of copending Application No. 10/712,642 for the same reasons of record set forth in the Office action mailed 6-2-04.

No arguments were made addressing this rejection.

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

Rejections Necessitated by Amendments

Applicant's arguments with respect to claims 1, 2, 15,16 and 18-24 have been considered but are moot in view of the new ground(s) of rejection.

Applicants argue that the 102 and 103 rejections mailed in the previous office action of 6-2-04 were improper because the prior art cited pertained to mouse, and not human, DNA-PK subunits. Applicants have since amended the claims to read on human and not mouse DNA-PK target genes. Accordingly, the new rejections are set forth below that address the amended claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 15 is rejected under 35 U.S.C. 102(b) as being anticipated by Connelly et al.

Connelly et al (Gene 175: 271-273, 1996) teach an antisense oligonucleotide that specifically hybridizes with human DNA-PK subunit, Ku70 (figure 2 on p. 273). The antisense oligonucleotide taught by Connelly et al

meets all of the structural limitations of the instantly claimed invention, and therefore would necessarily be presumed to have the functionality claimed, of specifically inhibiting expression human Ku70 in vitro.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 15,16 and 18-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Connelly et al as applied to claim 15 above, and Reeves et al, in view of Milner et al, Taniguchi et al and Au-Young et al (USPN 5,773,580).

The claims are drawn to compositions and methods for increasing a target cell's sensitivity to DNA damaging agents in vitro comprising the administration of an antisense oligonucleotide (and ribozyme) specifically targeting a nucleic acid encoding a human DNA dependent protein kinase subunit, which antisense inhibits the expression of the target human DNA PK catalytic or Ku70 subunit, and which antisense is in an appropriate expression vector, operably linked to a heat shock promoter, and optionally linked to a ribozyme.

Connelly et al is relied upon as cited in the 102 rejection above.

Reeves et al (J. Biol. Chem., Vol. 264(9): 5047-5052, 1989) teach the polynucleotide sequence encoding human DNA-PK subunit Ku70 (see figure 4 on p. 5050).

The primary references of Connelly et al and Reeves et al do not teach methods for increasing a target cell's sensitivity to DNA damaging agents in vitro comprising the administration of an antisense oligonucleotide specifically targeting a nucleic acid encoding a human DNA dependent protein kinase subunit, and which antisense is in an appropriate expression vector, operably linked to a heat shock promoter, and optionally linked to a ribozyme.

Milner et al (Nature Biotech. 15: 537-541, 1997) teach methods of designing and testing antisense oligonucleotides for their ability to specifically hybridize and inhibit the expression of a target nucleic acid of known nucleotide sequence in vitro (See especially figures 5-7 on pages 539-540).

Takiguchi et al (Genomics 35: 129-135, 1996) teach antisense oligonucleotides that specifically hybridize and inhibit expression of a DNA-PK subunit (see page 130, last paragraph on the left, first paragraph on the right). Taniguchi et al teach the role of DNA-PK in DNA repair, and an increase in a cell's sensitivity to DNA damaging agents with loss of DNA-PK function (see page 129, right col).

Au-Young et al teach pharmaceutical compositions comprising antisense oligonucleotides for inhibiting a known target gene, as well as teaching expression vectors comprising antisense oligonucleotides and ribozymes, which

oligonucleotides are operably linked to regulatory elements including an inducible (heat shock) promoter (see esp. col. 10-11, 20-21).

It would have been obvious to one of ordinary skill in the art to design and utilize antisense oligonucleotides to inhibit the expression of a human DNA dependent protein kinase subunit in vitro, because the sequences of the subunits for human DNA dependent protein kinase had been taught previously by Connelly et al and Reeves et al and Milner et al teach the ability to design and assess antisense oligonucleotides for their ability to inhibit the expression of a target gene of known nucleotide sequence in vitro using routine screening assays that are well known in the art (see Milner at pages 539-540). It would have been obvious to one of ordinary skill in the art to inhibit the expression of the known sequences encoding the subunits of human DNA dependent protein kinase of known nucleotide sequence in vitro using antisense oligonucleotides because the methods for inhibiting a target gene of known sequence using antisense had been taught previously by Milner et al and such methods of screening antisense in vitro for inhibition of target gene expression were routine at the time the invention was made. Milner et al additionally teach methods of designing and evaluating antisense which target different regions of a target gene of previously disclosed sequence for their ability to inhibit a target gene in vitro. One of ordinary skill in the art would have expected that the methods of designing and assessing antisense oligonucleotides for inhibiting a target gene of known sequence, which were taught by Milner et al, to be routine for a previously characterized target gene, would successfully be used to identify numerous

antisense oligonucleotides human DNA dependent protein kinase subunits, including KU70.

It would have been obvious to one of ordinary skill in the art to insert antisense oligonucleotides into an appropriate expression vector, operably linked to an inducible promoter including a heat shock promoter, because such expression systems have been used routinely in the art for expression of nucleic acid constructs including antisense and ribozymes in an appropriate target cell, as taught previously by Au-Young et al. One of ordinary skill in the art would have been motivated to operably link an antisense oligonucleotide to an inducible promoter in an appropriate expression vector in order to control the conditions of expression of the operably linked antisense, and in order to control conditions for antisense expression and subsequent inhibition of the antisense's target gene in an appropriate target cell.

One of ordinary skill in the art would have been motivated to target and inhibit the expression of DNA-PK in order to increase a target cell's sensitivity to DNA damaging agents (e.g. a target cancer cell), because Taniguchi et al teach the relationship between increasing cell radiosensitivity or loss of DNA repair function, and loss of functional DNA-PK. One of ordinary skill in the art would have expected that by utilizing appropriate conditions for expression (e.g. induction by heat), the antisense targeting DNA-PK would be expressed upon induction of the heat shock promoter because such induction systems as heat shock promoters have been routinely used as described by Au-Young et al. One of ordinary skill in the art would have been motivated to induce expression of

antisense and ribozymes under desired conditions (e.g. upon exposure heat) because induction is a way of controlling the conditions for increased expression of the operably linked antisense and ribozymes, and also a way of controlling the subsequent inhibition of target gene expression following expression of these antisense. In this way, increasing a cell's sensitivity to DNA damaging agents is in turn induced following heat treatment and expression of antisense. Therefore the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is **703-872-9306**. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(571) 272-0765.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (571) 272-0760. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (571) 272-0564. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR

system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JZ
12-15-04

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